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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/464,767 | 12/16/1999 | GERALD WAYNE BOTH | 50179-073 | 8030 |

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| EXAMINER | |
|---|---|
| PRIEBE, SCOTT DAVID | |
| **ART UNIT** | **PAPER NUMBER** |
| 1632 | |

DATE MAILED: 11/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/464,767 | BOTH ET AL. | |
| | Examiner | Art Unit | |
| | Scott D. Priebe | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *25-29,31-37 and 39-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *25-29,31,32,48,50 and 51* is/are allowed.

6)☒ Claim(s) *36,37,39-47 and 49* is/are rejected.

7)☒ Claim(s) *33-35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/14/04 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Claim Objections*

Claims 33-35 are objected to because of the following informalities. Claim 33 (from which claims 34 and 35 depend) recites "non-essential for to replication" in the last two lines; "to" should be deleted. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

Claims 36, 37, 39-47, and 49 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record set forth in the Office action of 4/16/04 and/or the new reasons set forth below concerning the amendments to claims 41, 42, 47 and 49. The claim(s) contains subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 36, 37, 39, 40, 42-47 and 49 are directed to or require a plasmid or adenoviral vector which comprises: 1) first or second nucleotide sequence; and 2) a third nucleotide sequence. As the claims are written, the third nucleotide sequence must be outside of and separate from the adenoviral genome, i.e. the third sequence is not inserted into the adenoviral genome. For example, if the third sequence were inserted into the SEQ ID NO: 3, the resulting DNA would not be SEQ ID NO: 3 and the vector or plasmid would not comprise SEQ ID NO: 3. The specification discloses plasmids which contain an adenoviral genome and a marker gene as separate, adjacent parts, e.g. pOAV100, or contain an adenoviral genome wherein the bacterial vector is inserted into the adenoviral genome, e.g. pOAV287Cm. The first could meet the claim limitations, whereas the second cannot. The specification also describes a viral vector comprising a non-adenoviral sequence, encoding a polypeptide or RNA, inserted into an ovine adenoviral vector genome. However, this disclosed embodiment also is not embraced by the claims, since it would not comprise the recited first or second sequence. This part of the rejection would be overcome by amending claims 36, 42, 45, 47 to recite that the third nucleotide sequence is inserted into the first or second nucleotide sequence, wherein the third sequence is inserted into a region not essential to replication of the adenoviral genome in ovine cells, as has been done for claims 33 and 41. In claim 49, the second sequence may either be within the first sequence (e.g. pOAV287Cm) or third sequence (e.g. pOAV100). Claim 49 should be amended to indicate that the second sequence (origin of replication) is inserted into the third sequence, i.e. outside the

adenoviral genome, or inserted into a region of the first sequence not essential to replication of the first sequence as an adenovirus in ovine cells, i.e. part of the adenoviral genome.

Claims 41, 42 and 47 have been amended to limit claimed method to one of "inducing an immune response in a mammal." Applicant points to pages 1 and 23 as supporting this amendment. However, page 1, lines 3-10, only indicates broadly that the invention is for delivery of nucleic acids expressing functional RNA or polypeptides to animals, and does not mention the purpose of inducing an immune response. Lines 11-36 of page 1 presents a discussion of the prior art, not a description of the invention, and cannot be used to support the new claim language. *Tronzo v. Biomet Inc.,* 47 USPQ2d 1829, 1833 (Fed. Cir. 1998).

The specification at page 23, line 29 to page 24, line 2 states:

> The viral vectors of the present invention can be used for the delivery and expression of therapeutic genes in grazing animals. In species which are not normally infected by ovine adenoviruses the lack of pre-existing immunity should allow efficient infection, gene delivery and expression. The genes may encode vaccine antigens, molecules which promote growth in production animals, molecules which modify production traits by manipulating hormone responses and other biologically active or therapeutic molecules.

Page 23 does not indicate that the vectors are to be used to generally induce an immune response. Further it does indicate that the vector is to be used in "grazing animals," which is presumed to mean grazing mammals, not to mammals in general. Also, the only description here that potentially relates to "inducing an immune response in a mammal" is the teaching that the vector may carry genes for "vaccine antigens," not polypeptides in general, and certainly not RNA and "RNA molecule" as recited in claim 47. While the vector and methods described in the specification would have enabled one of skill in the art to carry out the method of claims 41-44 when combined with their knowledge of the prior art either for inducing an immune response to a non-adenoviral polypeptide (or to the adenovirus itself), the specification itself not describe the

broad method now being claimed in such terms indicate it was contemplated by Applicant. Rather the specification describes a method for delivering vaccine antigens to grazing animals (mammals) for vaccination, which one of skill in the art would understand to mean to produce a protective immune response in a grazing mammal against the pathogen to which the "vaccine antigen" is directed, not simply a generic immune response to a generic polypeptide in a generic mammal. It is unclear how the specification even remotely supports delivering a vector encoding an RNA for the purpose of inducing an immune response.

Claim 49 has been amended to indicate that "said plasmid" is capable of replicating autonomously as an adenovirus. However, this is not what the specification teaches, nor has Applicant indicated where the specification describes such a plasmid. The specification teaches a plasmid comprising a bacterial origin of replication linking the ITRs of an adenoviral genome but separate from the adenoviral genome (i.e. the second nucleotide sequence would be part of the third nucleotide sequence not the first) or a plasmid comprising an adenoviral genome containing the second nucleotide sequence inserted into a region that is non-essential for replication of the adenoviral genome in sheep cells. An adenoviral genome replicates as a linear molecule, hence the purpose of the third nucleotide sequence of the plasmid. The plasmid is cut in the third sequence before transfecting sheep cells releasing a linear DNA comprising the adenoviral genome, and upon replication in sheep cells the remnant of the third sequence will be removed. In other words, the plasmid will not (and cannot) replicate as an adenovirus, only the first sequence (which is presumed to include the second sequence) will replicate as an adenovirus. It is suggested that "said plasmid" be replaced with --the first nucleotide sequence--.

Claim 47 remains rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 16 Sep. 2002 as modified below, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim as amended is directed to a method for producing an immune response in a mammal by administering an adenoviral vector that encodes an RNA molecule. The only description of RNA encoded by a vector is a functional RNA that is a messenger RNA, antisense RNA or ribozyme (page 5, lines 1-7). The specification teaches that the disclosed adenoviral vectors are primarily for use in grazing animals, presumably this means grazing mammals, for the purpose of vaccination, gene therapy, or genetic engineering to promote growth or modify production traits (page 23). Of these only, the claim appears to apply only to vaccination. With the exception of mRNA encoding to antigenic proteins and peptides derived from pathogenic organisms for vaccines, the specification provides no guidance on what, antisense sequences or ribozymes should be encoded by the exogenous DNA sequence present in the viral vectors used. The specification provides no working examples of any of these uses. The specification does present evidence that the vector lacking an exogenous DNA sequence can infect and propagate in sheep.

The prior art shows that adenoviral vectors, particularly those based on HAV types 4, 5 and 7 encoding antigenic polypeptides have been used to generate full or partial protective immunity in a variety of for varying lengths of time in a variety of non-human mammals against rabies, hepatitis B, vesicular stomatitis virus, herpes simplex virus and Epstein Barr virus. See Imler (Vaccine 13(13): 1143-1151, 1995), which reviews the state of the prior art on adenoviral

vector-based vaccines. Surprisingly, however, an HAV type 7 recombinant viral vector that could induce protective immunity to hepatitis B in chimpanzees, did not even result in the production of antibodies against the HBsAg expressed from the vector in humans (see Imler, page 1147, col. 2), showing some unpredictability with respect to the target mammal (note that this result was originally published in 1992, see Ref. 54 in Imler). Also, as discussed above the specification shows that based on the dramatic structural and sequence dissimilarity between the OAV287 genome and the genomes of other well-characterized mammalian adenoviruses, OAV287 is quite a different virus than the HAV viruses on which the prior art adenoviral vaccines are based. Therefore, one cannot predict whether OAV287-based vectors would be suitable substitutes for the prior art HAV-based vectors of the prior art vaccines.

With respect to producing an immune response against an antisense RNA or ribozyme, the specification fails to teach a utility for doing so. Furthermore, there is no evidence of record from the specification or the prior art that expression of an antisense RNA or ribozyme in a mammal would, or even could, produce an immune response against the RNA. The specification also fails to describe how to use the claimed method for producing an immune response against a non-adenoviral polypeptide that is not from a pathogen in grazing animals.

Given little or no guidance on *in vivo* applications in the specification and the lack of working examples, the high unpredictability of the art of *in vivo* DNA transfer in general with and with a new, untried vector specifically in using the vectors for vaccines it would require undue experimentation to practice the invention *in vivo*.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe

Scott D. Priebe
Primary Examiner
Art Unit 1632